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L4: Entry 1 of 1 File: JPAB Oct 6, 1998

PUB-NO: JP410265359A
DOCUMENT-IDENTIFIER: JP 10265359 A
TITLE: PREVENTIVE FOR WRINKLE FORMATION

PUBN-DATE: October 6, 1998

INVENTOR-INFORMATION:
NAME
TSUJI, NAOKO
MORIWAKI, SHIGERU
IMOKAWA, GENJI
SUZUKI, YASUTO
NISHIZAWA, YOSHINORI

ASSIGNEE-INFORMATION:

NAME	COUNTRY
KAO CORP	N/A

APPL-NO: JP09071698
APPL-DATE: March 25, 1997

INT-CL (IPC): A61K 7/48; A61K 7/00

ABSTRACT:

PROBLEM TO BE SOLVED: To obtain a preventive for wrinkle formation, capable of preventing and improving the occurrence of wrinkle caused by aging of skin by including a metal-dependent elastin decomposing inhibitor as an active ingredient.

SOLUTION: This medicine comprises a metal-dependent elastin decomposing inhibitor, especially a metal-dependent elastin decomposing inhibitor derived from a fibroblast of corium, such as a phosphonic acid derivative or a mercaptopropionamide derivative as an active ingredient. The medicine is further formulated with an ultraviolet absorber or an ultraviolet controller to preferably prepare a skin preparation for external use. The formulated amount of the metal-dependent elastin decomposing enzyme inhibitor in the case of preparing the skin preparation for external use is preferably 0.0001-5 wt.% based on the whole composition. The elastin decomposing enzyme includes one belonging to a serine protease and one belonging to a metal-dependent protease. An elastase inhibitor belonging to the metal protease has excellent controlling action on wrinkle formation.

WEST

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L5: Entry 1 of 1 File: DWPI Dec 8, 1998

DERWENT-ACC-NO: 1998-531686
DERWENT-WEEK: 199908

TITLE: Preventives against skin ageing such as wrinkles, sags, loss of skin tension - contain phosphoric acid derivative or its salt, or mercapto:propionamide derivative or its salt

INVENTOR: IMOKAWA, G; MORIWAKI, S ; NISHIZAWA, Y ; SUZUKI, Y ; TSUJI, N

PATENT-ASSIGNEE:

ASSIGNEE	CODE
KAO CORP	KAOS

PRIORITY-DATA:

1997JP-0071700	March 25, 1997
1997JP-0071698	March 25, 1997
1997JP-0071699	March 25, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 10324611 A	December 8, 1998	N/A	006	A61K007/00
WO 9842308 A1	October 1, 1998	J	023	A61K007/48
JP 10265359 A	October 6, 1998	N/A	006	A61K007/48
JP 10265360 A	October 6, 1998	N/A	006	A61K007/48

DESIGNATED-STATES: US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
JP10324611A	March 10, 1998	1998JP-0058038	N/A
WO 9842308A1	March 18, 1998	1998WO-JP01143	N/A
JP10265359A	March 25, 1997	1997JP-0071698	N/A
JP10265360A	March 25, 1997	1997JP-0071700	N/A

INT-CL (IPC): A61K 7/00; A61K 7/42; A61K 7/48

ABSTRACTED-PUB-NO: WO 9842308A
BASIC-ABSTRACT:

A preventive for skin aging contains phosphoric acid derivs represented by formula R1-(OH)P(=O)-NHCH(R2)CONHCH(R3)COOH (I) or its salts.

Alternatively, it contains a metal-dependent-type elastic-decomposition enzyme inhibitor contg mercapto-propionamide deriv or its salt as a major component.

In (I), R1-3 = H, hydrocarbon group which may be substituted, or sucrose residual group.

USE - The preventive is used for cosmetic preparations such as skin lotions, skin creams etc..

ADVANTAGE - The preventive prevents formation of wrinkles and sags and decreases of skin tension.

ABSTRACTED-PUB-NO: WO 9842308A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/0

DERWENT-CLASS: D21 E19
CPI-CODES: D08-B09A; E05-G04; E05-G05; E05-G06; E07-H; E10-C04;

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DB Name	Query	Hit Count	Set Name
USPT,JPAB,EPAB,DWPI	$mercaptopropionamide same hair	5	L12
USPT,JPAB,EPAB,DWPI	phosphonic same hair	21	L11
USPT,JPAB,EPAB,DWPI	phosphonic same (elastase or neutral endopeptidase)	8	L10
USPT,JPAB,EPAB,DWPI	phosphonic and (elastase or neutral endopeptidase)	75	L9
DWPI	phosphonic and (elastase or neutral endopeptidase)	2	L8
DWPI	WO-9842308-$.did.	1	L7
DWPI	WO 9842308-$.did.	0	L6
DWPI	JP-10265359-$.did.	1	L5
USPT,JPAB,EPAB,DWPI	$mercaptopropionamide and (elastase or neutral endopeptidase)	1	L4
USPT,JPAB,EPAB,DWPI	$mercaptopropionamide and hair	7	L3
USPT,JPAB,EPAB,DWPI	$mercaptoproprionamide and hair	0	L2
USPT,JPAB,EPAB,DWPI	mercaptoproprionamide and hair	0	L1

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                                  ENTRY   SESSION
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INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA,
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    BIOBUSINESS, BIOCOMMERCE, BIOSIS,
BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
    CANCERLIT, CAPLUS, CEABA, CEN, CIN,
CONFSCI, CROPB, CROPU, DDFB, DDFU,
    DGENE, DRUGB, DRUGLAUNCH,
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ENDOPROTEASE)

      1 FILE BIOSIS
      2 FILE BIOTECHNO
      5 FILE CAPLUS
      1 FILE CEABA
      1 FILE DDFB
 22 FILES SEARCHED
      3 FILE DDFU
      1 FILE DRUGB
      6 FILE DRUGU
      1 FILE EMBASE
      1 FILE ESBIOBASE
      1 FILE LIFESCI
 42 FILES SEARCHED...
      2 FILE MEDLINE
      1 FILE SCISEARCH
      2 FILE TOXLIT
     34 FILE USPATFULL

 15 FILES HAVE ONE OR MORE ANSWERS,  56
FILES SEARCHED IN STNINDEX

L1   QUE (MERCAPTOPROPIONAMIDE OR
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ENDOPROTEA
     SE)

=> D RANK

F1      34  USPATFULL
F2       6  DRUGU
F3       5  CAPLUS
F4       3  DDFU
F5       2  BIOTECHNO
F6       2  MEDLINE
F7       2  TOXLIT
F8       1  BIOSIS
F9       1  CEABA
F10      1  DDFB
F11      1  DRUGB
F12      1  EMBASE
F13      1  ESBIOBASE
F14      1  LIFESCI
F15      1  SCISEARCH


=> FILE F2-15

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=> S L1

L2        24 L1

=> DUP REM L2

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L3        14 DUP REM L2 (10 DUPLICATES REMOVED)
             ANSWERS '1-6' FROM FILE DRUGU
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ANSWERS '7-9' FROM FILE CAPLUS
ANSWER '10' FROM FILE BIOTECHNO
ANSWERS '11-12' FROM FILE TOXLIT
ANSWER '13' FROM FILE CEABA
ANSWER '14' FROM FILE DRUGB

=> S L3 AND PY 1998

3 FILES SEARCHED...
5 FILES SEARCHED...
6 FILES SEARCHED
9 FILES SEARCHED...
L4 9 L3 AND PY 1998

=> D BIB AB 1-9

L4 ANSWER 1 OF 9 DRUGU COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1995-15089 DRUGU C P B
TI Phosphorous acid analogs of L-680,833, a potent monocyclic beta-lactam
inhibitor of human leukocyte elastase.
AU Durette P L; Chabin R M; Fletcher D S; Green B G; Hanlon W A; Humes J L;
Knight W B; Lanza T J Jr; Mumford R A; Pacholok S; MacCross M
CS Merck-USA
LO Rahway, N.J., USA
SO ; Bioorg.Med.Chem.Lett. (5, No. 3, 271-74, 1995) 1 Tab. 7 Ref.
CODEN: ; BMCL
AV Department of Medicinal Chemical Research, Merck Research Laboratories,
PO Box 2000, Rahway, NJ 07065-0900, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The synthesis and inhibitory activity against human leukocyte
elastase (HLE) of several phosphorus acid analogs of L-680833 (1)
are reported. The compounds and their corresponding ethyl esters were
found to be potent and time-dependent inhibitors of HLE in-vitro.
Cellular activity was demonstrated by inhibition of the generation of the
N-terminal cleavage product A-alpha-(1-21) from the A-alpha chain of
fibrinogen in whole blood stimulated with A-23187 The compounds were,
however, only weakly active when dosed orally in the hamster lung
hemorrhage assay

L4 ANSWER 2 OF 9 DRUGU COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1992-18583 DRUGU B
TI Substrate and Inhibitor Studies on Proteinase 3.
AU Kam C M; Kerrigan J F; Dolman K M; Goldschmeding R; Borne A E G K von
dem; Powers J C
LO Atlanta, Georgia, United States; Amsterdam, Netherlands
SO FEBS Lett. (297, No. 1-2, 119-123, 1992) 2 Fig. 2 Tab. 27 Ref.
CODEN: FEBLAL ISSN: 0014-5793
AV School of Chemistry and Biochemistry, Georgia Institute of Technology,
Atlanta, GA 30332, U.S.A.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AB Substituted isocoumarins (IC) were potent in-vitro inhibitors of the
esterolytic activity of proteinase 3 (PR-3) extracted from healthy human
blood neutrophils. The best inhibitor was 3,4-diCl-IC. Peptide
phosphonates and peptide chloromethyl ketones were poor inhibitors of
PR-3 Peptide thioesters were good substrates for PR-3. A comparison of
the activities of PR-3 with those previously reported for human
neutrophil elastase (HNE) indicated that there are differences in the
extended substrate binding sites and the catalytic residues. Thioester
substrates and IC inhibitors should be useful for further studies on the
functional role of PR-3 in-vivo and in-vitro.

L4 ANSWER 3 OF 9 DRUGU COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1991-17340 DRUGU P B C
TI Irreversible Inhibition of Serine Proteases by Peptide Derivatives of
(alpha-Aminoalkyl)phosphonate Diphenyl Esters.
AU Oleksyszyn J; Powers J C
LO Atlanta, Georgia, United States
SO Biochemistry (30, No. 2, 485-93, 1991) 2 Fig. 4 Tab. 32 Ref.
CODEN: BICHAW ISSN: 0006-2960
AV School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia
30332, U.S.A.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AB 20 Peptidyl (alpha-aminoalkyl)-phosphonate diphenyl esters (APDE; see
formula sheet) with substrate-related sequences were synthesized and
found to be specific irreversible inactivators of serine proteases
including bovine chymotrypsin (BC), porcine pancreatic elastase (PPE),
human leukocyte elastase (HLE), cathepsin G (CG) and rat mast cell
protease II (MCP). The inhibitor-enzyme complexes were extremely stable.
All the tri-and tetrapeptide phosphates (8-21) were more potent
inhibitors than the simple benzyl oxycarbonyl derivatives (1-7).The
inhibitory potency was dependent on the amino acid sequence of the
peptide. The APDE were chemically stable, stable in plasma and did not
react with AChE.

L4 ANSWER 4 OF 9 DRUGU COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1989-14882 DRUGU P B
TI Molecular Drug Research: A Review of Mechanism Directed Serine Protease
Inhibitors.
AU Demuth H U; Neumann U
LO Halle, Germany,East
SO Pharmazie (44, No. 1, 1-11, 1989) 5 Tab. 153 Ref.
CODEN: PHARAT ISSN: 0031-7144
AV Domplatz 1, Halle (Saale), DDR-4020.
LA German
DT Journal
FA AB; LA; CT
FS Literature
AB A review of the biospecific drug design of inhibitors of serine

proteases, as exemplified by trypsin, chymotrypsin, plasmin and
elastases , is presented. A range of different types of inhibitor
have been developed, including affinity labeling inhibitors, transition
state inhibitors, acyl enzyme inhibitors (inverse substrates) and enzyme
activated inhibitors (suicide substrates). Various classes of compound,
which are represented by these inhibitor categories are discussed and
methods for determination of the kinetics of enzyme inhibition are
surveyed. Structure activity considerations allied to modern analytical
methods (high resolution NMR, crystallography, computer graphics) have
resulted in highly selective inhibitors, which may lead to new
therapeutic and diagnostic agents.

L4 ANSWER 5 OF 9 DRUGU COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1983-38312 DRUGU P B C
TI Aminoalkylphosphonofluoridate Derivatives: Rapid and Potentially
Selective Inactivators of Serine Peptidases.
AU Lamden L A; Bartlett P A
LO Berkeley, California, United States
SO Biochem.Biophys.Res.Commun. (112, No. 3, 1085-90, 1983) 1 Tab. 16 Ref.
CODEN: BBRCA9 ISSN: 0006-291X
AV Dept. of Chemistry, University of California, Berkeley, California 94720,
U.S.A.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AB ***Phosphonic*** acid analogs of N-Cbz-alanine and
N-Cbz-phenylalanine were converted to ester and amide fluoridates. The
compounds, 16 and 2, which mimic the natural peptide substrates, were
the most potent inactivators of ***elastase*** and alpha chymotrypsin
yet found.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2000 ACS
AN 1996:599235 CAPLUS
DN 125:247628
TI
2-(2-Oxo-1,2-dihydro-1-pyridyl)-N-[3,3,3-trifluoro-1-(lower alkyl)-2-oxopropyl]acetamide derivatives as inhibitors of human leukocyte
elastase
IN Bernstein, Peter R.; Shaw, Andrew; Thomas, Royston M.; Warner, Peter;
Wolanin, Donald J.
PA Zeneca Limited, UK
SO U.S., 70 pp. Cont.-in-part of U.S. Ser. No. 869,993,abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5521179	A	19960528	US 1993-45009	19930408 --
ZA 9302697	A	19931028	ZA 1993-2697	19930416 --

PRAI GB 1991-8357 19910418
GB 1991-8358 19910418
GB 1992-5392 19920312
GB 1992-8379 19920416
GB 1992-8380 19920416
US 1992-869993 19920416
US 1992-869993 19920416
GB 1992-14448 19920708
GB 1992-17362 19920814
GB 1992-17363 19920814
GB 1992-17364 19920814
OS MARPAT 125:247628
AB The present invention relates to certain novel heterocyclic amides which
are 1-pyridylacetamide compds. I wherein: R0 is C1-5 alkyl; R = e.g., H,
acyl, sulfonyl; R5 and R6 = e.g., H, lower alkyl, B-Y where B is aryl or
heteroaryl and Y is a direct bond, methylene, ethylene, or trans-vinylene
(with proviso), which are inhibitors of human leukocyte elastase (HLE),
also known as human neutrophil elastase (HNE), making them useful whenever
such inhibition is desired, such as for research tools in pharmacol.,
diagnostic and related studies and in the treatment of diseases in mammals
in which HLE is implicated. The Ki values for I which were tested are
generally on the order of 10-7 M or much less. The invention also
includes intermediates useful in the synthesis of these heterocyclic
amides, processes for prepg. the heterocyclic amides, pharmaceutical
compns. contg. such heterocyclic amides and methods for their use. Thus,
e.g., acetophenone was formylated and cyclized with cyanoacetamide to
provide 6-phenylpyrid-2-one-3-carbonitrile; hydrolysis to the carboxylic
acid followed by urethane formation yielded 3-benzyloxycarbonylamino-6-
phenylpyrid-2-one; alkylation of the latter with N-(2-tert-
butyldimethylsilyloxy-3,3,3-trifluoro-1-isopropylpropyl)-2-iodoacetamide
(prepn. given) followed by deprotection and oxidn. afforded
2-(3-benzyloxycarbonylamino-2-oxo-6-phenyl-1,2-dihydro-1-pyridyl)-N-(3,3,3-
trifluoro-1-isopropyl-2-oxopropyl)acetamide (I; R Cbz, R5 = H, R6 Ph,
R0 = iso-Pr).

L4 ANSWER 7 OF 9 BIOTECHNO COPYRIGHT 2000 Elsevier Science B.V.
AN 1993:23153203 BIOTECHNO
TI Patent selections
SO Current Opinion in Therapeutic Patents, (***1993***), 3 5 (667-673)
CODEN: COTPES ISSN: 0962-2594
DT Journal; Note
CY United Kingdom
LA English

L4 ANSWER 8 OF 9 CEABA COPYRIGHT 2000 DECHEMA
AN 1996:167810 CEABA
TI Catalytic reaction mechanism-based design of low-molecular inhibitors of
proteolytic enzymes
Projektowanie niskoczasteczkowych inhibitorow enzymow proteolitycznych na
podstawie znajomosci mechanizmu katalizowanej reakcji
AU Kafarski, P.; Gancarz, R. (Wroclaw TU, 50-370

Wroclaw, Poland)
SO Wiad. Chem. (***1996***) 50(1 2), p.53-76, 18f,2t,33l
CODEN: WICHAP ISSN: 0043-5104
DT Journal
LA Polish
AB Practical aspects of designing the reaction mechanism-based inactivators
of proteolytic cysteine, serine, aspartyl and metalloprotease enzymes
were discusseed. The chemistry of interactions between a variety of
peptide inhibitors especially with ***phosphonic*** , sulfonic,
sulfoxide, ketone or aldehyde groups (leucopeptine, fluorophosphate,
bestatine, zinc complexants) and papaine, catepsin G, chymotrypsin,
elastase , HIV virus protease, carboxypeptidase A or thermolysine
enzymes as a base for drug designing was outlined. For instance, the
inhibition of renine and angiotensine-converting enzyme with BPP5
oligopeptide from Bothrops jararaca lizard venom gave an assumption for
designing commercial captopril und cilazapril antihypertonicums. Paper
was given at the 5th Symposium on Peptide Conformation and Protein
Structure, Karpacz, Poland, 29 April to 2 May 1995. (Polaczek)

L4 ANSWER 9 OF 9 DRUGB COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1978-41233 DRUGB B
TI ORGANOPHOSPHORUS COMPOUNDS AS ACTIVE SITE-DIRECTED INHIBITORS OF
ELASTASE.
AU NAYAK P L; BENDER M L
LO EVANSTON,ILL.,USA.
SO BIOCHEM.BIOPHYS.RES.COMMUN. (83, NO.3, 1178-82, ***1978***)
DT Journal

=> INDEX BIOSCIENCE

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS SINCE FILE TOTAL
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FULL ESTIMATED COST 26.15 38.45

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INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, AQUASCI,
BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
CANCERLIT, CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU,
DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 16:11:26 ON 28 JUL 2000

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24 FILES SEARCHED...
1 FILE DRUGB
1 FILE EMBASE
17 FILE IFIPAT
3 FILE JICST-EPLUS
1 FILE MEDLINE
50 FILES SEARCHED...
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1 FILE TOXLINE
8 FILE TOXLIT
277 FILE USPATFULL
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21 FILE WPINDEX

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L5 QUE (MERCAPTOPROPIONAMIDE OR PHOSPHONIC)(L)(HAIR)

COST IN U.S. DOLLARS SINCE FILE TOTAL
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FULL ESTIMATED COST 3.60 42.05

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
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CA SUBSCRIBER PRICE 0.00 -0.56

=> D RANK

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F5 17 IFIPAT
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F10 1 DRUGB
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F2 9 CAPLUS
F3 2 IFIPAT
F4 1 BIOSIS
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F7 1 MEDLINE
F8 1 SCISEARCH
F9 1 TOXLINE
F10 1 TOXLIT
F11 1 WPIDS
F12 1 WPINDEX

=> FILE F2-12

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ANSWERS '10-11' FROM FILE IFIPAT
ANSWER '12' FROM FILE WPIDS

=> S L8 AND PY<1998

3 FILES SEARCHED...
4 FILES SEARCHED...
6 FILES SEARCHED...
7 FILES SEARCHED...
8 FILES SEARCHED...
=> ------User Break------>
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SEARCH ENDED BY USER

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LOG Y

COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 61.80 110.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY SESSION
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STN INTERNATIONAL LOGOFF AT 16:46:35 ON 28 JUL 2000